Halocarbons have been impugned as the main cause of ozone depletion. These include both chlorofluorocarbons (CFCs) and halons. Both are short carbon chains, CFCs being saturated with predominantly chlorine and halons with bromine. Chlorofluorocarbons largely result from manufacturing processes, including those involving air-conditioning coolants, foam extrusion, and industrial solvents. Halons come from both natural sources, such as seawater, and industrial processes involving fire extinguishers.

When halocarbons reach the stratosphere, they act as a catalyst for the destruction of ozone. The chlorine and bromine are not consumed. Each chlorine molecule has a half-life of 75 years and may destroy about 100,000 molecules of ozone.

Although somewhat controversial, there is a fair consensus that the ozone layer is thinning. Satellite measurements report worldwide ozone depletion of at least 3% since 1978, with some estimates substantially higher. This depletion is unevenly distributed, being as much as 50% at the poles and about 7% in the temperate areas. No ozone depletion has been reported in the equatorial regions. There is an important seasonal variation, with ozone levels being lowest in the winter and highest during the summer.

Increased amounts of UV radiation, especially UVB, will reach the earth's surface as a result of ozone depletion. It is estimated that for every 1% decrease in ozone, there will be a 2% to 6% increase in the incidence of both basal cell and squamous cell carcinoma. More important, it is estimated that there will be about a 1% increase in the incidence of melanoma for each 1% depletion in ozone. As ultraviolet light is also implicated in causing cataracts, as many as 2.8 million additional cataracts could occur worldwide by 2075.

Despite the documented decreased ozone levels, no increases in ground-level UVB had been recorded in temperate regions until a recent report. For the first time, UVB levels in a temperate region have been shown to be increasing by 5% per year since 1988. There have also been recent intermittent reports of increased UVB at ground levels in the Antarctic. The cold temperature at the poles may predispose to the ozone depletion and the resultant increased UVB.

There are some reassuring factors. Smog, pollution, and particulate material in the atmosphere all help to absorb or disperse UVB. Indeed, some models even predict decreased UVB levels at ground level despite ozone depletion. Further, even if the amount of UVB doubled or tripled in northern and southern latitudes, these areas would receive less UVB than the equatorial regions currently receive. Seasonal ozone variation is also partially protective. Ozone is created by photochemical interactions, so as UV irradiation increases—that is, summertime—increasing amounts of ozone are produced.

Approaches to dealing with ozone depletion include phasing out all ozone-damaging halocarbons by the year 2000, following an international agreement signed in 1988 by 42 countries. This should decrease the amount of artificial halocarbons in the atmosphere, although the effect of natural halocarbons such as from the eruption of Mount Pinatubo in the Philippines is unknown. Chlorofluorocarbon substitutes are being actively developed, although at the present time they appear to be more expensive and less efficient in industrial processes. The recycling of CFCs in compounds such as home and auto coolants is becoming mandatory in most states. Many new cars are using an air-conditioning system free of CFCs. Finally, risks posed by increased UVB at the earth's surface can be partially offset by protective measures such as sunscreens, eyewear, and appropriate clothing.

KEVIN L. WELCH, MD
Tucson, Arizona

REFERENCES

Coldiron BM: Thinning of the ozone layer: Facts and consequences. J Am Acad Dermatol 1992; 27:653-662

Grant-Kels JM: The impact of ozone depletion on the skin. Pediatr Dermatol 1993; 10:81-83

McCally M, Cassel CK: Medical responsibility and global environment change. Ann Intern Med 1990; 113:467-473

Recent Developments in the Treatment of Human Papillomavirus

WARTS HAVE BEEN RECOGNIZED since Greek and Roman times. Despite recent advances in recombinant DNA technology, which have allowed the identification of more than 60 different genotypes of human papillomavirus (HPV), current treatment remains controversial and often disappointing.

With recent polymerase chain technology, HPV DNA can be identified in tissues without clinically apparent lesions (so-called subclinical lesions). Dormant HPV has been identified in tissues using this technology (latent lesions). Our failure to cure HPV infections, many think, results from our inability to resolve these lesions. Unfortunately, few studies demonstrate consistent resolution of subclinical and latent lesions by any treatment method.

Recently the malignant transformation potential of HPV has come to the forefront and several questions have been raised, not only about the malignant potential of clinical HPV lesions, but also about subclinical and latent lesions. Papillomavirus types 6, 11, 16, and 18 have been implicated as a possible cause of condylomata acuminata (genital warts). More important, HPV types 6 and 11 have been associated with low-grade dysplasia of the cervix, whereas types 16 and 18 are associated with high-grade dysplasia, carcinoma in situ, and invasive carcinomas of the cervix. Human papillomavirus types 6, 11, 16, and 30 have been detected in laryngeal squamous cell carcinomas. Some lesions of epidermodysplasia verruciformis (a rare, chronic skin disorder associated with HPV types 5, 8, 14, 17, and 20) are thought to undergo transformation to squamous cell carcinoma.

Concerns about HPV tumorigenicity and unacceptable recurrence rates with standard treatment methods (cryosurgery, carbon dioxide laser, electrosurgery, surgery, salicylic acid, trichloroacetic acid, podophyllin, fluorouracil [5-fluorouracil], and bleomycin sulfate) led to the search for other therapeutic options.

Interferons are cytokines—immunoregulatory proteins

secreted by cells—possessing antiviral activity. Initial reports in 1974 described promising results in the management of HPV plantar warts with the use of interferon alfa ointment. A multicenter trial using parenterally administered interferon showed that only 19 of 77 patients with genital warts had the complete clearance of lesions. Other centers have reported better success rates (as high as 53%) with parenteral interferon, but at doses where patients had more side effects. This apparently narrow therapeutic window led to the use of intralesional interferon alfa. A multicenter, double-blind, placebo-controlled trial using intralesional interferon alfa showed that 62% of treated patients were completely free of lesions, in contrast to 21% in the control group. More important, 75% of complete responders remained free of lesions 18 months after therapy, and side effects were substantially reduced. An interesting note is that one study found that 50% of patients given interferon had concomitant improvement in untreated lesions. This study suggests that intralesional interferon may reduce subclinical and latent lesions that are instrumental in the recurrence, as well as persistence, of HPV. One study suggests that intralesional interferon has an effect on HPV-associated cervical intraepithelial neoplasia and, in some cases, can achieve complete resolution of lesions. We are several studies away from proving a clear advantage of this drug in the treatment of HPV, but data so far indicate that it may provide an alternative to the disappointing recurrence rates and malignant transformation currently experienced.

Another possible therapy is the systemic use of retinoic acid, which may have potential for reducing recurrence and malignant transformations by preventing infectivity by HPV. One study has shown that physiologic concentrations of retinoic acid suppressed the infectivity of HPV in human keratinocytes, as well as the proliferation of previously infected human keratinocytes. The use of etretinate resolved extensive warts in immunosuppressed patients.

Although several therapeutic options are available in the treatment of HPV, no one method offers a clear advantage. Commonly used treatments, although offering convenience and cost savings, do not, in general, reduce recurrence rates, and they fail to address the issue of malignant transformation. The therapies described in this epitome could provide more acceptable recurrence rates and lower tumorigenicity, but there simply are not enough supportive data at this time. Furthermore, the relationship between HPV and cancer is an evolving area and, as it becomes more clearly defined, so should our treatment strategies.

SUSAN SHIMOMAYE, MD
Oceanside, California

REFERENCES

Khan MA, Jenkins GR, Tolleson WH, Creek KE, Pirisi L: Retinoic acid inhibition of human papillomavirus type 16-mediated transformation of human keratinocytes. Cancer Res 1993; 53:905-909

Quan MB, Moy RL: The role of human papillomavirus in carcinoma. J Am Acad Dermatol 1991; 25:698-705

Trofatter KF: Interferon treatment of anogenital human papillomavirus-related diseases. Dermatol Clin 1991; 9:343-352

α-Hydroxy Acids for Skin Rejuvenation

α-HYDROXY ACIDS are organic acids naturally found in fruits (malic, citric, and tartaric acids), sugar cane (glycolic acid), and sour milk (lactic acid).

In the 1970s, these acids were reported to decrease corneocyte adhesion, allowing removal of the thick scale of ichthyosis, psoriasis, and seborrheic keratoses. In higher concentrations, epidermolysis (splitting of the epidermis from the dermis, or "peeling") occurs. Because they lack systemic toxicity, concentrated α-hydroxy acids began to be used by dermatologists in place of other peeling agents such as phenol, trichloroacetic acid (TCA), and resorcinol to treat photoaging, especially to reduce hyperpigmentation and fine wrinkles, to remove early actinic and seborrheic keratoses, and to give the skin improved texture and a youthful glow—in other words, as agents for freshening peels.

The proposed mechanisms of these improvements include thinning of the stratum corneum, dilatation of superficial blood vessels, and thickening of the actinically thinned epidermis and upper (papillary) dermis. Recent work suggests that α-hydroxy peels stimulate mast cell degranulation. It is hypothesized that the liberated mast cell products can stimulate dermal fibroblasts to produce increased amounts of collagen and elastin, regenerating youthful-appearing skin.

One method of treatment is to apply an α-hydroxy acid in a 20% to 70% concentration to skin that has been pretreated with a 5% to 10% solution of α-hydroxy acid or tretinoin (Retin-A) for two to four weeks and then scrubbed with acetone, alcohol, soap and water, or an α-hydroxy acid cleanser. The depth of peel depends on the time of exposure, whether the acid is buffered or unbuffered, the vigor of preparation, sebaceous gland activity of the patient, and personal idiosyncrasy. This is considered a superficial or very superficial peel. Repeated peels at weekly or monthly intervals may give improvement comparable to mid-depth TCA peels with less pain and crusting than the single, more intense peel.

Most clinicians feel that postinflammatory hypopigmentation and hyperpigmentation are less than with phenol or TCA, but there is greater patient-to-patient variability with α-hydroxy acids, so peels must be done cautiously at first. Dark-skinned patients are at a higher risk for pigmentary problems. Because the depth of penetration is time-related, overexposure to α-hydroxy acids used in peels can result in severe burning with subsequent scarring.

It has yet to be determined if the reversal of photoaging by α-hydroxy acid peels is nonspecific or can be duplicated by any method that causes chronic low-grade inflammation such as dilute TCA, tretinoin, salicylic acid, resorcinol, carbon dioxide slush, and epidermabrasion with rough-surfaced pads, sponges, pumice stones, or scrubbing granules.

In addition to the use of α-hydroxy acids in high concentration for in-office peeling, lotions and creams